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DDT/DDE and Infant Exposure

The article by López-Carrillo et al. (*1*), which discusses the public health implications of using DDT in Mexico, is a welcome contribution to the literature. DDT is a public health concern not only in the countries still using the chemical but also in those countries that have restricted, phased out, or banned use of the chemical. Presently, it is difficult to conclude if DDT contributes to breast cancer incidence, and the lack of complete confidence in our understanding of the relationship between this xenoestrogen and breast cancer should not prevent us from finding alternatives to DDT that have less public health impact. López-Carrillo et al. (*1*) base their concern for DDT primarily on the possible increase of breast cancer with exposure. Although this endpoint is of concern, toxicological endpoints that deserve equal attention pertain to infant exposure.

Teratology studies by Eriksson et al. (*2–4*) have investigated neurological and developmental endpoints in neonatal mice. Although work is still required to elicit the nature of low-dose DDT damage to the central nervous system in neonates, the results of their work suggest that 1) the neonatal period of brain development may be similar to other perinatal periods in which the brain is susceptible to xenobiotic compounds and 2) susceptibility to damage by DDT and similar-acting compounds may be greatest during the height of rapid brain growth and during the rapid development of muscarinic acetylcholine receptors in the cerebral cortex (*2–5*).

Although a direct comparison between the 10-day-old mice used in these studies and 10-day-old humans cannot be made, the sequence of events of brain development between humans and rodents is quite similar (*6,7*) That is, nerve production, myelin formation, receptor development, etc., are events that occur in the same order in rodents and humans (*7*). At day 10, mice are in their last stages of neuron production for the hippocampus and cerebellum (*8*). Antimitotic drugs are much more toxic if exposure occurs earlier in development when more neurons are being produced (*9,10*). However, the first 2 weeks of postnatal life in the rodent are a period of rapid development of synaptic connections, transmitter systems, and myelination. During this stage of brain development, exposure to teratogens leads to disruption of some or all of these events, resulting in permanent injury. For example, metals such as lead, cadmium, and organotin can injure the brain at this stage, as can hypothyroidism (*11*). The applicability of these teratology study results to the human situation will continue to become clearer as future findings delineate effects at developmental time points when mice are more sensitive and when the development of rodent and human neurosystems are similar.

It was with the consideration of this previously described experimental work that a breast milk study was initiated in the state of Washington to access a population of concern consisting primarily of low-income Hispanics. We conducted this study to 1) determine actual levels of DDT and DDE in breast milk of mothers residing in the Yakima River basin; 2) assess the relative impact of fish consumption on the total DDT/DDE body burden; and 3) determine if total DDT and DDE levels received by breast-feeding infants were elevated to potentially deleterious levels. Fish collected from the Yakima River between 1989 and 1991 had DDT and DDE levels among the highest recorded in the United States (*12*). We were concerned that mothers who frequently consumed Yakima River bottom-feeding fish could have breast milk DDT and DDE concentrations sufficiently high to expose their infants to potentially deleterious levels of these compounds. Among the 36 individuals sampled (12 individuals for each of three cohorts: fish consumers, Mexico-born nonconsumers, and U.S.-born nonconsumers); results indicated that fish consumption did not significantly increase DDT/ DDE breast milk concentrations. However, as has been reported elsewhere, subjects born in Mexico had significantly elevated levels of DDT and DDE ($p < 0.01$) in breast milk compared to levels found in subjects born in the United States (*1,13,14*).

For each cohort sampled, an infant DDT intake level was determined using the breast milk value that included two-thirds of that particular cohort. For a 5-kg infant consuming 1 kg breast milk daily, infant DDT intake levels for the cohorts were in the range of $0.7–3.5 \times 10^{-3}$ mg/kg/day. These results do not include two outliers from the Mexico-born nonconsumer cohort who had DDT/DDE levels greater than two standard deviations from the mean. Our infant exposure values derived from the cohort data (excluding outliers) were more than two orders of magnitude below the administered dose used by Eriksson et al. (*2–4*). The two women (considered outliers) had DDT breast milk levels that correspond to the elevated levels observed in women living in Mexico. These DDT breast milk levels would expose breast-feeding infants each day to levels that are less than two orders of magnitude from the one-time administered dose given to neonatal mice.

Although DDT may contribute to an increase in breast cancer, exposure to DDT may also produce neurological and developmental endpoints of significance that require consideration. The study conducted in Washington State and data on breast milk DDT levels obtained from women in Mexico indicate that infants may be exposed to potentially deleterious levels of these compounds through breast milk. With DDT in our environment, various populations can still be exposed to sufficiently elevated DDT levels in the United States that warrant concern. Also, due to the influx of Mexico-born women into the United States, their U.S.-born infants may be a population of concern. Future research in this area should consider the feasibillty of detecting these neurological and developmental outcomes in individuals that have been previously exposed as infants, and not just for those living in areas where DDT is still in use but also in countries or areas where use has been banned or severly restricted.

Koenraad Mariën
Office of Environmental Health
Assessment Services
State of Washington Department of Health
Olympia, Washington

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Lead in Drinking Water: A Preventive Solution

Many children are at risk from lead (Pb) poisoning. One study found that one in five children in North Carolina had tested positive for elevated levels of Pb in their blood (*1*). In a separate study in Missouri, it was reported that 5.7% of 528 schools and 2.4% of 1,123 day care centers exceeded the EPA's action level of Pb in drinking water (*2*). These numbers and conclusions justify major concern, and efforts to curtail Pb consumption should be rigorously investigated.

One source that certainly contributes to this widespread problem is permanently installed drinking water fountains (*3*); of notable concern are water fountains found in elementary schools (*1,2,4*). Many old school buildings probably contain Pb-contaminated supply pipes or Pb solder from which the Pb leaches into drinking water and is then passed into human tissues, causing various physiological and neurological damage. As water in these buildings rests in Pb-contaminated plumbing overnight, throughout the summer months, and during school vacations when there is little movement of water, Pb accumulates and levels increase, causing a potential health threat. However, leaching of Pb is unpredictable, and strategies for the elimination of it from drinking water have been difficult to develop and evaluate. Although various approaches have been devised to reduce Pb in water to safe levels, i.e., adding calcium carbonate and legislating stringent Pb piping standards, these endeavors are not sufficient for complete safety (*3*) Temporary efforts to reduce Pb concentration in drinking water include morning flushing of the water source or permanently installed water coolers (*1*), use of Pb filters, or switching to bottled water dispensed in free-standing coolers. It has been reported that one-time morning flushing of drinking water coolers in elementary schools may not provide day-long Pb exposure protection for children (*4*). Flushing is tedious and time consuming and offers only temporary reduction of Pb because, in many cases, the Pb leaches back into the water from Pb-contaminated plumbing; therefore, many people have switched to bottled water dispensed in free-standing coolers. Until recently, it was not known whether chemical contaminants such as Pb would accumulate in bottled water dispensed in free-standing coolers.

We have examined bottled water dispensed from free-standing coolers and found Pb levels to be less than 5 ppb without any evidence of Pb accumulation in water remaining in contact with the plastic plumbing materials and the stainless steel water reservoir cooling tank during periods of non-use up to 28 days (unpublished observations). These free-standing water coolers with plastic plumbing and a stainless steel cooling tank may be one way to provide school children with Pb-free drinking water.

Bill Jirles
Julius Thigpen
Diane Forsythe
National Institute of Environmental Health Sciences
Research Triangle Park, North Carolina

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Calculation of Cancer Risk

Recently the EPA proposed changes in how it determines which chemicals and pollutants cause cancers, relying less on animal tests and more on new techniques of molecular biology. Acknowledging recent advances in molecular biology and other fields, EPA's new proposal would give more weight to a broad range of evidence, including details about precisely how toxic agents wreak their harm on human cells and on genetic material that control cells' reproduction. By taking the mechanics of cancer into account, the new approach will more precisely measure a chemical's cancer potential. At the same time, the new proposal opens the way for new statistical analyses about the effects that chemicals might have at very small doses that people are exposed to, rather than at very large doses given to animals to test their effects.

In summary, the EPA will rightly draw more on improved understanding of the mechanism by which toxic effects are produced. Over the years it has been recognized that the ultimate value of toxicological information relates to its use in the development of formal risk or safety assessments. Thus, a broad array of research is focused on the development of mechanistic information that will have value in assessing the potential human health risk of environmental pollutants and consumer products and assessing the safety of pharmaceuticals.

From this research have emerged significant advances in our understanding of the mechanism of carcinogenesis, which justifies EPA's effort to rethink cancer calculations. Among these advances are the following:

- Significant developments in science of how humans metabolize cancer-causing substances. Most molecules identified as carcinogenic do not produce their detrimental effects themselves. They have to be metabolized, usually into a form that can react irreversibly with sites on DNA, altering gene expression. The role of two important sets of enzymes—the